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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,528	10/13/2000	David M. Stern	0575/62096/JPW/JML	8939

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John P. white
Cooper & Dunham, LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 09/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/687,528	Applicant(s) STERN ET AL.	
	Examiner Shin-Lin Chen	Art Unit 1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 22 August 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *3-5 and 11-14*.
   Claim(s) withdrawn from consideration: *None*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

S Chen

Shin-Lin Chen
Primary Examiner
Art Unit: 1632

Continuation of 11. does NOT place the application in condition for allowance because: Applicants argue that the specification provides the DNA and amino acid sequences for murine, bovine and human RAGE and even if there is experiment required to practice the claimed invention, no undue experimentation is required (reply, p. 2-3). This is not found persuasive because of the reasons or record. Although the amino acid sequences of murine, bovine and human RAGE were known, however, the specification only provides the biological function of mouse soluble RAGE but fails to provide adequate guidance and evidence whether the soluble RAGE of human or bovine origin or other species would have the same biological function as that of the mouse sRAGE. The claims encompass using numerous sRAGEs, which have different amino acid sequences, derived from various organisms, such as humans, cows, horses, rats, mice, sheep, other mammals, fishes, insects etc., to prevent exaggerated restenosis in a diabetic subject in vivo. No detailed information for the structural feature of sRAGE that contributes to prevent exaggerated restenosis has been provided. Sine the amino acid sequences of sRAGE derived from different organisms would vary and the biological function of a protein was unpredictable from mere amino acid sequence at the time of the invention, one skilled in the art at the time of the invention would not know whether those different sRAGEs would have the same biological function as the mouse sRAGE to reduce the smooth muscle proliferation and migration in carotid artery. Therefore, it would require one skilled in the art undue experimentation to practice over the full scope of the invention claimed. Applicants argue that sRAGE homologs from different species are not the same as splice variants and no evidence has been shown that different sRAGEs would behave differently (reply, p. 3-4). This is not found persuasive because of the reasons of record. The phrase "the same stretch of an amino acid sequence can contribute to different biological functions in different proteins" by examiner does not mean the splice variants, rather it was reported by Davis, G., 1990 (The New Biologist, Vol. 2, No. 5, pp. 410-419). Davis points out that EGF repeats is present in an extraordinarily diverse group of molecules, such as growth factors, transmembrane molecules, extracellular matrix proteins, and soluble secreted proteins and it is often difficult to deduce what contribution it makes to a totally unrelated protein. As discussed above, there is no evidence of record that shows sRAGE derived from various organisms would have the same function as the mouse sRAGE. Applicants argue that the fatty Zucker rat used in the present invention has diseased arteries and the statement by Park is to avoid conclusively stating that the fatty Zucker rat model reflects all pathophysiological characteristics observed in diabetic human subjects (reply, p. 5). This is not found persuasive because of the reasons of record. As reported by Miller, significant interspecies and intraspecies differences were found to exist among the various animal models, particularly with respect to the extent and composition of neointimal thickening, drug and lipid metabolism, and the activity of coagulation and fibrinolytic systems. The amount of elastin in the media of coronary arteries of larger animals, such as dogs, pigs and baboons, are very similar to that of the human coronary artery but greater than that in small species, such as rodents and fowls, and thickness of the arterial intima varies among species. "Rat arteries differ morphologically from human arteries in that they have no vasa vasorum, have a very much thinner subintimal layer and have a relatively small elastin content in the media (e.g. p. 421, left column, lines 4-7). Although the statement by Park could be scholarly caution, however, such statement reflects ths state of the art regarding the relevance of restenoic animal models to human restenosis, which is unknown. Although fatty Zucker rat model has disease arteries and is a well-established model for type II diabetes, however, whether the data of fatty Zucker rat regarding the use of a drug or sRAGE to prevent exaggerated restenosis is predictive of the therapeutic effect of the drug or sRAGE in a diabetic human subject is still unknown. Thus, the claims remain rejected under 35 U.S.C. 112 first paragraph.